

Claims

1. A combined preparation for simultaneous, separate or
5 sequential use as a contrast agent in ultrasound
imaging, said preparation comprising:
 - i) an injectable aqueous medium having gas dispersed
therein; and
 - ii) a composition comprising a diffusible component
10 capable of diffusion *in vivo* into said dispersed
gas so as at least transiently to increase the
size thereof.
2. A combined preparation as claimed in claim 1 wherein
15 the dispersed gas comprises air, nitrogen, oxygen,
carbon dioxide, hydrogen, an inert gas, a sulphur
fluoride, selenium hexafluoride, an optionally
halogenated silane, a low molecular weight
hydrocarbon, a ketone, an ester, a halogenated low
20 molecular weight hydrocarbon or a mixture of any of
the foregoing.
3. A combined preparation as claimed in claim 2 wherein
25 the gas comprises a perfluorinated ketone,
perfluorinated ether or perfluorocarbon.
4. A combined preparation as claimed in claim 3 wherein
the perfluorocarbon comprises a perfluoroalkane,
perfluorocalkene or perfluorocycloalkane.
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5. A combined preparation as claimed in claim 2 wherein
the gas comprises sulphur hexafluoride or a

perfluoropropane, perfluorobutane or perfluoropentane.

6. A combined preparation as claimed in any of the preceding claims wherein the dispersed gas is stabilised by a coalescence-resistant surface membrane, a filmogenic protein, a polymer material, a non-polymeric and non-polymerisable wall-forming material or a surfactant.
- 10 7. A combined preparation as claimed in claim 6 wherein said surfactant comprises at least one phospholipid.
- 15 8. A combined preparation as claimed in claim 7 wherein at least 75% of the said surfactant material comprises phospholipid molecules individually bearing net overall charge.
- 20 9. A combined preparation as claimed in claim 8 wherein at least 75% of the film-forming surfactant material comprises one or more phospholipids selected from phosphatidylserines, phosphatidylglycerols, phosphatidylinositols, phosphatidic acids and cardiolipins.
- 25 10. A combined preparation as claimed in claim 9 wherein at least 80% of said phospholipids comprise phosphatidylserines.
- 30 11. A combined preparation as claimed in any of the preceding claims wherein the composition comprising the diffusible component is formulated for administration cutaneously, subcutaneously,

intramuscularly, intravenously or by inhalation.

12. A combined preparation as claimed in any of claims 1 to 10 wherein the composition comprising the diffusible component further comprises a carrier liquid.

13. A combined preparation as claimed in claim 12 wherein the diffusible component is dispersed in an aqueous carrier liquid in the form of an oil-in-water emulsion or microemulsion.

14. A combined preparation as claimed in claim 13 wherein the diffusible component comprises an aliphatic ether, polycyclic oil, polycyclic alcohol, heterocyclic compound, aliphatic hydrocarbon, cycloaliphatic hydrocarbon or halogenated low molecular weight hydrocarbon.

15. A combined preparation as claimed in claim 14 wherein the diffusible component comprises a perfluorocarbon.

16. A combined preparation as claimed in claim 15 wherein the perfluorocarbon comprises a perfluoroalkane, perfluoroalkene, perfluorocycloalkane, perfluorocycloalkene or perfluorinated alcohol.

17. A combined preparation as claimed in claim 16 wherein the diffusible component comprises perfluoropentane, perfluorohexane or perfluorodimethylcyclobutane.

18. A combined preparation as claimed in any of claims 13

to 17 wherein the emulsion is stabilised by a phospholipid surfactant.

19. A combined preparation as claimed in claim 18 wherein
5 at least 75% of the said phospholipid surfactant comprises molecules individually bearing net overall charge.

20. A combined preparation as claimed in claim 19 wherein
10 at least 75% of the phospholipid surfactant is selected from phosphatidylserines, phosphatidylglycerols, phosphatidylinositols, phosphatidic acids and cardiolipins.

15 21. A combined preparation as claimed in claim 20 wherein at least 80% of said phospholipid surfactant comprises phosphatidylserines.

22. A combined preparation as claimed in any of the
20 preceding claims which further includes a vasodilator drug.

23. A combined preparation as claimed in claim 22 wherein
said vasodilator drug is adenosine.

25 24. A combined preparation as claimed in any of claims 1 to 21 which further includes a therapeutic agent.

26 25. A combined preparation as claimed in any of claims 1 to 21 which further includes contrast-enhancing moieties for an imaging modality other than ultrasound.

26. A method of generating enhanced images of a human or non-human animal subject which comprises the steps of:

5 i) injecting a physiologically acceptable aqueous medium having gas dispersed therein into the vascular system of said subject;

10 ii) before, during or after injection of said aqueous medium administering to said subject a composition comprising a diffusible component capable of diffusion *in vivo* into said dispersed gas so as at least transiently to increase the size thereof; and

15 iii) generating an ultrasound image of at least a part of said subject.

27. A method as claimed in claim 26 wherein the composition comprising the diffusible component is administered cutaneously, subcutaneously, intramuscularly, intravenously or by inhalation.

28. A method as claimed in claim 26 or claim 27 wherein a vasodilator drug is coadministered to the subject.

29. A method as claimed in claim 28 wherein said vasodilator drug is adenosine.